1: IARC Sci Publ 1997;(142):281-9

The use of biological markers as predictive early-outcome measures in epidemiological research.

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One of the possible uses of biomarkers in epidemiological research is as early-outcome measures to predict the occurrence of clinical disease and to elucidate the biological mechanism of pathogenesis. This use is conceptually less straightforward than the well established use of biomarkers to improve or extend exposure assessment or to study interindividual variations in disease susceptibility. In principle, this form of use could accelerate or otherwise facilitate etiological research. However, in practice, the recent review literature suggests that this mode of biomarker use, especially in cancer epidemiology, is the least clear-cut and the least well developed. The recurrent problem is identifying biomarkers that: (1) are on the causal pathway, (2) have a high probability of progression to clinical disease, and (3) account for all or most of the cases of the specified clinical outcome. Such biomarkers would be most useful if they conferred a long lead-time relative to clinical disease occurrence.

Publication Types:
- Review
- Review, Tutorial

PMID: 9354927 [PubMed - indexed for MEDLINE]

1: Int J Vitam Nutr Res 1996;66(1):3-18

Intermediate cancer biomarkers and their use in beta-carotene studies in humans.

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The most effective means of avoiding the development of squamous cell carcinomas is the elimination of risk factors such as tobacco smoke and alcohol and of exposure to occupational and dietary carcinogens. In addition, chemoprevention by micronutrients such as beta-carotene may be promising. However, studies verifying such effects using cancer incidence or mortality as study endpoint are extremely costly of financial and manpower resources. Therefore, premalignant intermediate biomarkers such as histological lesions (dysplasias/leukoplakias/ polyps), genetic changes (DNA damage, mutations) or enzymatic changes (protein kinase C or ornithine decarboxylase activation) are increasingly being used as surrogate endpoints. Even though most preneoplastic biomarkers still need to be verified and shown to be linked to malignancy, their use in clusters may enhance their predictability. In human trials beta-carotene has reversed some lesions such as micronuclei, leukoplakias and dysplasias in the oral cavity, whereas other lesions, e.g. colorectal polyps (i.e. their recurrence after resection) have not been found to respond. But proliferation markers in the colon mucosa have been modified by beta-carotene. Preliminary findings are also available of a potential reduction of esophageal dysplasias in a high-risk Chinese population and of cervical dysplasias in a group of American women. The available beta-carotene data are sufficiently encouraging to justify continuation of trials using intermediate cancer markers.

Publication Types:

- Review
- Review, Tutorial

PMID: 8698542 [PubMed - indexed for MEDLINE]

1: Ann Thorac Surg 1995 Aug;60(2):466-72 Related Articles, NEW Books, LinkOut

ELSEVIER SCIENCE FULL-TEXT ARTICLE

Survival in early-stage non-small cell lung cancer.

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The duration of survival in early-stage lung cancer (stages I and II) varies between reports in the literature. Several reasons account for this: patient population heterogeneity, inconsistent staging, anatomic variability, dissimilar tumor morphology, and unpredictable tumor biology. This report addresses some of the issues in early-stage non-small cell lung cancer that relate to variability between estimates of survival in end stage reporting. We review several large series since the introduction of the International Staging System in 1986 and other selected, contemporary reports that address end results in patients with pathologic stage I or stage II lung cancer. Overall survival for patients with pathologic stage I disease is 64.6% (range, 55% to 72%) and 41.2% for patients with stage II disease (range, 29% to 51%). Reducing morphologic differences by placing patients in groups based on the TNM subset and refinement in categorization by matching TNM subsets based on histology and other factors can improve considerably homogeneity and enhance prognostic predictability. The development of more accurate measures for predicting prognosis may serve to clarify the roles of primary and adjuvant treatment, particularly in those patients with early-stage disease associated with poor prognostic factors in whom the potential for long-term survival is reduced.

Publication Types:
- Review
- Review, Tutorial

PMID: 7646126 [PubMed - indexed for MEDLINE]

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1: Curr Oncol Rep 2001 Jul;3(4):368-75

CURRENT reports

Transcription factors and other dysregulated proteins in melanoma prognosis.

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Approximately one third of patients with cutaneous melanoma later develop a metastatic disease, having then an extremely poor rate of survival. Because of the highly unpredictable nature of melanomas, finding those patients who are likely to develop a metastatic disease and those patients who probably will survive is an ongoing challenge. The current "conventional" prognosticators, such as Breslow thickness, Clark level of invasion, and ulceration, cannot perfectly predict the clinical course of this disease at an individual level. Although the sentinel lymph node biopsy procedure and reverse transcription polymerase chain reaction techniques have significantly improved the staging of patients with melanoma, new molecular prognostic markers may help in selection of appropriate patients for strenuous adjuvant therapies and for randomized clinical trials. Furthermore, these markers also improve our basic understanding of the biology of cutaneous melanoma, potentially offering new targets for novel treatment strategies. This paper reviews the current literature on transcription factors and other dysregulated proteins involved in melanoma prognosis.

Publication Types:
- Review
- Review, Tutorial

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